were added in a previous amendment. Claims 69 and 70 are cancelled in the present amendment. These cancellations are made without acquiescing to the Examiner's rejections, but are made to further prosecution and Applicant's business interests. Applicant reserves the right to prosecute Claims 69 and 70 (or similar claims) in the future. Claims 45-48 and 71 are presently amended. Therefore, Claims 45-68 and 71 are currently pending.

In the Office Action dated July 8, 2003 the Examiner has made three rejections. The currently pending rejections are:

1) Claims 46-48, 71 stand rejected under 35 U.S.C. 112, first paragraph;

2) Claims 45-68, 71 stand rejected under 35 U.S.C. 112, second paragraph; and

3) Claims 45, 48-68, 71 stand rejected under 35 U.S.C. 102(b).

Applicant believes that the pending Claims are fully supported, definite, and are not taught by the prior art. Therefore Claims 45-68, 71 should be passed into allowance.

REJECTIONS

For clarity, the rejections at issue are set forth by number in the order they are herein addressed.

I. THE SPECIFICATION FULLY SUPPORTS THE CLAIMS

The Examiner has rejected Claims 46-48, and 71 under 35 U.S.C. 112, first paragraph ". . . as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." (Office Action 7/8/2003, page 3). Applicant respectfully disagrees. The Examiner argues: "The amendment fails to point to any support in the specification for the newly added language. However, the specification does not appear to describe or discuss "a computer readable medium" and a "decision tree". The concept of a computer readable medium" and a "decision tree" does not appear to be part of the originally filed invention. Therefore a computer readable medium" and a "decision "tree" constitutes new matter. Applicant is required to cancel the new matter in reply to this office action." (Office Action 7/8/2003, page 3.)

To the contrary, the Specification provides ample, specific and detailed support for the Claims. Several non-limiting examples are provided below:

"Assays for detection of polymorphisms or mutations fall into several categories, including, but not limited to direct sequencing assays, fragment polymorphism assays, hybridization assays, and ***computer based data analysis.***" (Specification, II. "Assays for Generating Genomic Profiles", page 40. Emphasis added.)

"In some embodiments of the present invention, ***perioperative genomic profiles are generated using computer-based data analysis*** of a genetic information sample (e.g., stored nucleic acid sequence information). A sample is collected from a subject at anytime (e.g., at birth), sequence information is generated (e.g., through DNA sequencing), and ***the information is stored (e.g., as digital information on a portable chip)***. During the perioperative period, ***the subject's sequence information is scanned by a computer program*** for the pre-selected markers. A report (e.g., a perioperative genomic profile) is generated." (Specification II.E., "Computer-Based Data Analysis", page 49. Emphasis added.)

"In some embodiments of the present invention, ***the data is generated, processed, and/or managed using electronic communications systems*** (e.g., Internet-based methods). In some embodiments, ***a computer-based analysis program*** is used to translate the raw data generated by the genomic profile (e.g., the presence or absence of a given SNP or mutation) into data of predictive value for the clinician (e.g., probability of abnormal pharmacological response, presence of underlying disease, or differential diagnosis of known disease)." (Specification, III. "Analysis and Delivery of Data", page 50. Emphasis added.)

"Where the sample comprises previously determined genetic information (e.g., sequence information, SNP or mutation information, etc.), the information may be directly sent to the genomic profiling service by the subject (e.g., a information card containing the genetic information may be ***scanned by a computer and the data transmitted to a computer*** of the genomic profiling center using an electronic communication systems). Once received by the genomic profiling service, the sample is processed and a genomic profile is produced (i.e., genomic data), specific for the medical

or surgical procedure the subject will undergo." (Specification, III. "Analysis and Delivery of Data", pages 50-51. Emphasis added.)

"In some embodiments, the process of selecting markers, ***performing detection assays***, and distributing data to subjects and clinicians is organized by an ***integrated electronic (e.g., web-based) system.***" (Specification, "Detailed Description of the Invention", page 30. Emphasis added.)

"The present invention contemplates ***any method capable of receiving, processing, and transmitting the information to and from medical personal and subject.***" (Specification III., "Analysis and Delivery of Data", page 50. Emphasis added.)

"In some preferred embodiments of the present invention, the information generated by perioperative ***genomic profiling is distributed in a coordinated and automated fashion.***" (Specification III. "Analysis and Delivery of Data, page 49. Emphasis added.)

"The fate of the sample and genomic data is driven by the subject, who is given a menu (e.g. ***electronically***) of choices. . . . For example, using an ***electronic communication system***, the central facility can provide data to the clinician, the subject, or researchers. . . . In some embodiments, the subject may be able to directly access the data using the ***electronic communication system.***" (Specification III. "Analysis and Delivery of Data, page 51. Emphasis added.)

"The data may be displayed to the clinician by any suitable method. For example, in some embodiments, the genomic profiling service generates a report that can be printed for the clinician (e.g., at the point of care) or ***displayed to the clinician on a computer monitor***." (Specification III., "Analysis and Delivery of Data", page 51. Emphasis added.)

"The data generated by the assay may converted to a ***genomic profile in a computer system*** of the emergency vehicle or may be ***transmitted to distant computer system for processing.***" (Specification III., "Analysis and Delivery of Data, page 51. Emphasis added.)

In order to further the prosecution of the present case, while not acquiescing to the Examiner's argument, and retaining the right to prosecute the original claims (or similar

claims) in the future, Applicant has amended Claims 46-48 and 71 to recite "computer program" and "information to optimize perioperative care".

In view of the above, Applicant requests that these rejections be withdrawn.

II. THE CLAIMS ARE DEFINITE

The Examiner has rejected Claims 45-68 and 71 under 35 U.S.C. 112, second paragraph ". . . as being indefinite for failing to particularly point out and distinctly claim the subject mater which the applicant regards as the invention." (Office Action 7/8/2003, page 4.) The Examiner argues: "The response asserts that the claimed reagents provide agents for detecting the variant alleles using the range of different technologies described in the specification." This argument has been thoroughly reviewed, but is not found persuasive because the claim does not require that the reagents in fact detect the presence of the variant alleles. The claim could be amended to recited "reagents which detect . . . " to overcome the rejections."

Applicant respectfully disagrees. However, in order to further the prosecution of the present case, while not acquiescing to the Examiner's argument, and retaining the right to prosecute the original claims (or similar claims) in the future, Applicant has amended Claims 45 and 71 to recite "reagents which detect . . .", and "component parts which detect . . .", respectively.

In view of the above, Applicant requests that these rejections be withdrawn.

III. THE CLAIMS ARE NOT ANTICIPATED

The Examiner has rejected Claims 45, 48-68, and 71 under 35 U.S.C. 102(b) as being anticipated by the catalogs of three manufacturers: Boehringer Mannheim; Perkin Elmer; and Applied Biosystems. For clarity and efficiency, because their defects as prior art are shared, and because the Examiner has cut and pasted from the Boehringer Mannheim text of the Office Action verbatim to the Perkin Elmer and Applied Biosystems text of the Office Action, the three references will be addressed together.

The text of 35 U.S.C. 102 quoted by the Examiner reads:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application in the United States.

(Office Action 7/8/2003, page 5).

Applicant respectfully asserts that the references cited by the Examiner glaringly fail to meet this standard of anticipation. To the contrary, the prior art references do **not** teach a perioperative genomic profile kit. The prior art references do **not** teach reagents which detect the presence of variant alleles of two or more genes selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNF*α and *TNF*β. The prior art references do **not** teach instructions for using a kit for generating a perioperative genomic profile. The prior art references do **not** teach a kit having components that provide a subject-specific clinical pathway of medical intervention if used (see e.g., Claim 71).

The Federal Circuit has stated the relevant analysis for anticipation as follows:

"A claim is anticipated only if each and every element as set forth in the claims is found, either expressly or inherently described, in a single prior art reference."[1]

Applicant respectfully submits that not one of the catalog references cited by the Examiner teach each and every element as set forth in the claims.

In view of the above, Applicant requests that these rejections be withdrawn.

III. A. THE CLAIMS TEACH DETECTION OF SPECIFIC VARIANT ALLELES

In response to the 1/2/2003 Office Action, Applicant pointed out to the Examiner that: "None of the three references teaches variant alleles of the genes of the present invention. None of the three references teaches detection of variant alleles in two or more genes from the group of genes of the present invention." (Response to Office

[1] *Verdegaal Bros. V. Union Oil of California*, 2 USPQ2d 1051, 1053 (Fed.Cir. 1987)

Action, filed 5/11/2003, page 9). In the present Office Action the Examiner argues: "This argument has been thoroughly reviewed, but is not found persuasive because the claim does not require detection of the variant alleles." (Office Action 7/8/2003, page 8).

Applicant respectfully disagrees. However, in order to further the prosecution of the present case, while not acquiescing to the Examiner's argument, and retaining the right to prosecute the original claims (or similar claims) in the future, Applicant has amended Claims 45 and 71 to recite "reagents which detect . . .", and "component parts which detect . . .", respectively. None of the cited references teach or suggest kits having reagents that detect the specific variant alleles.

In view of the above, Applicant requests that these rejections be withdrawn.

III. B. INSTRUCTIONS ARE FUNCTIONAL COMPONENTS OF THE CLAIMED KITS AND CANNOT BE IGNORED

The Examiner has rejected Claims 45, 48-68, and 71 under 35 U.S.C. 102(b) as being anticipated by the catalogs of three manufacturers: Boehringer Mannheim; Perkin Elmer; and Applied Biosystems. Not one of the three prior art references recite "instructions for using said kit for generating said perioperative genomic profile for said subject." as recited in Claim 45, or the information to optimize perioperative care that, based at least on the presence or absence of variant alleles of two or more genes selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNF*α and *TNF*β measured by said kit, directs a user to a specific clinical pathway of medical intervention for said subject, as recited in Claim 71. Nevertheless, the Examiner persists in re-asserting a rejection under 35 U.S.C. 102(b) only by improperly ignoring these elements. (Office Action 7/8/2003, page 8).

The Examiner argues that "In re Haller states that, in accordance with the patent statutes, an article or composition of matter, in order to be patentable, must not only be useful but must be new. *If there is no novelty in an article or composition itself, then a patent cannot be properly granted on the article or composition regardless of the use for which it is intended.*" (Office Action 7/8/2003, page 9. Italics in original. Underline added.) In the immediately preceding Response to Office Action, Applicant pointed out

that the claimed instructions are novel, physical components dictating the manipulations of physical objects and activities which, as components of the claimed kits, implement a set of actions to accomplish a useful, concrete and tangible result. (Response to Office Action 5/11/2003, page 11). However, in the Office Action of 7/8/2003 the Examiner has conspicuously failed to respond to this statement of fact. Indeed, the Examiner concedes in the present Office Action that "The instructions are used to describe how the kit is intended to be used." (Office Action 7/8/2003, page 9. Emphasis added). Nevertheless, the Examiner continues to confuse In re Haller's "the use for which it is intended" (i.e. the kit's purpose), with "how the kit is intended to be used", i.e. the claimed and patentable instructions for operation of the present invention that embody functional components interacting with other components of the claimed kits in novel modes of cooperation, thereby permitting the kit's functionality to be realized.

In consideration of In re Gulack, the Examiner argues "in the case of In re Gulack, the printed matter is considered a patentable distinction because the function of the device depends upon the printed matter itself, which is a part of the substrate; without the printed indicia or numbers, the substrates lose their function. Such is not the case with the instantly claimed kit. The components of the kit remain fully functional absent the printed instructions for use." (Office Action 7/8/2003, page 9). The Examiner's mischaracterizations are erroneous, and unsupported by any evidence, affidavit or other authority. To the contrary, the claimed instructions of the present invention clearly result in a structural and manipulative differences (In re Casey) between the manufacturer's catalogs cited by the Examiner as prior art, and the articles and compositions of the present claims. Rather than remaining fully functional, the useful, concrete and tangible aspects of the kits of the present claims are not maintained after removal of "printed instructions for use".

Applicant submits herewith a Declaration of Morris Waxler, Ph.D. The Declaration explains that instructions for the use of an *in vitro* genetic diagnostic kit bear a critical functional relationship to the components of the kit, and that the function of an *in vitro* genetic diagnostic kit depends on the instructions. For example, without instructions approved by the Food & Drug Administration, the *in vitro* diagnostic kit is not considered functional by the Food & Drug Administration.

The Examiner argues "The intended use which is recited on the instructions lacks a functional relationship to the kit because the instructions do not physically or chemically affect the chemical nature of the components of the kit, and furthermore, the components of the kit can still be used by the skilled artisan for other purposes (as a whole or individually. Therefore, the kit is unpatentable over the prior art because they function equally effectively with or without instructions, and accordingly no functional relationship exists between the instructions for use and kit components." (Office Action 7/8/2003, page 10).

In these assertions the Examiner makes numerous errors of both fact and law. First, the Examiner's arguments are conclusory, and unsupported by any citation to relevant case law, the MPEP, an affidavit or other authority. Second, the Examiner once again confuses the "intended use which is recited on the instructions" with "printed instructions for use". That is, the Examiner confuses the "intended use" of a kit (its purpose) with "how to use" the kit (i.e. its operation with the physical component instructions of the claims). Indeed the Examiner tacitly acknowledges the difference in distinguishing "intended use which is recited on the instructions", from the body (how to) of the instructions. The claimed instructions of the present invention are not a "statement of intended use". In Claims 45 - 68 they are physical component parts of the Claims. For example, a claim to "A system of doing X, comprising component Y" is anticipated by prior art that discloses component Y for purposes other than X (i.e., use X is a statement of use the does not impart patentable weight to the claim). However, a claim that recites "A system comprising component Y and component Z, wherein component Z is configured to permit component Y to find use in process X" is patentable if the prior art does not teach the use of component Y in process X, or does not teach the use of component Z that is configured to facilitate the use of Y for X. The present claims represent the latter rather than the former example.

Third, abundant examples are proffered in the Specification of instructions which both chemically and physically affect the chemical nature of the components of the kit (See Section I.B. "Criteria for Selection of Markers", page 32, Section I.C. "Categories of Markers", page 34, Experimental Example 1 "Perioperative Genomic Screening for

Anesthesia Markers", page 53, Experimental Example 2 "Generation of Genomic Profiles", page 57.)

Fourth, the Examiner puts forward no relevant case law, MPEP citation, affidavit or other authority in which the legal test for a functional relationship rests on whether claims "physically or chemically affect the chemical nature of the components of the kit." (Office Action 7/8/2003, page 10). This is a standard the Examiner has made up and does not comport with the law.

Fifth, whether or not "the components of the kit can still be used by the skilled artisan for other purposes (as a whole or individually)", (Office Action 7/7/2003, page 10), has no legal bearing on patentability.

Sixth, the Examiner's unsupported statement that "the kit is unpatentable over the prior art because they function equally effectively with or without the instructions" is clearly erroneous. The Examiner repeats the identical mistake a second time in consideration of In re Miller stating "no functional relationship exists between the instructions and the other elements of the kit because the components of the kit are capable of functioning without the printed matter." (Office Action 7/8/2003, page 10) To the contrary, as evidenced by the Declaration of Morris Waxler, Ph.D., instructions for the use of an *in vitro* genetic diagnostic kit bear a critical functional relationship to the components of the kit, and that the function of an *in vitro* genetic diagnostic kit depends on the instructions. Without instructions approved by the Food & Drug Administration, the *in vitro* diagnostic kit is not considered functional by the Food & Drug Administration, (i.e. the Food & Drug Administration recognizes the importance of the instructions to enable use of the reagents, and use of data obtained by use of the reagents in the hands of practitioners). To sustain the rejection, the Examiner must present evidence (not conclusory statements or guesses) as to the lack of a functional relationship between the claimed instructions and other components of the kits. Nor has the Examiner cited authority for the Examiner's proposition that the test for a functional relationship is whether or not the components of the kit are capable of functioning without the printed matter. This is made-up law and does not reflect the actual law.

Finally, the Examiner argues that "Applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a

patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references." (Office Action 7/8/2003, page 11). To the contrary, in the Response to Office Action filed 5/11/2203 the Applicant expressly points out:

> "None of the three references teaches variant alleles of the genes of the present invention. None of the three references teaches detection of variant alleles in two or more genes from the group of genes of the present invention. None of the three references teaches categorical criteria for the selection of genes and variant alleles of the present invention. None of the three references teaches generation of a perioperative genomic profile." (Response to Office Action, 5/11/2003, page 9).

Applicant respectfully submits that the Boehringer Mannheim, Perkin Elmer, and Applied Biosystems catalog pages cited by the Examiner do not teach each and every element of the claims as required, and requests that the rejection under 35 USC §102 be withdrawn.

It is respectfully submitted that Applicant's claims as amended should be passed into allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application Applicant encourages the Examiner to call the undersigned collect at (608) 218-6900.

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